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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,588	07/25/2003	Laurence C. Eisenlohr	003252-53311-C	2965

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EXAMINER	
GUIDRY, GUY L	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,588	EISENLOHR ET AL.	
	Examiner	Art Unit	
	Guy Guidry, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,24 and 25* is/are pending in the application.

4a) Of the above claim(s) *8-16,24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/24/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is a First Office Action on the Merits. Receipt is acknowledged of a response filed 21 April 2006 to the Restriction Requirement mailed 28 March 2006. Preliminary amendments filed 24 October 2003 have been entered. Claims 1-16 and 24-25 are currently pending in this application.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-7, in the reply filed on 21 April 2006 is acknowledged. Claims 8-16 and 24-25 are withdrawn from further consideration by in accordance with 37 CFR 1.142(b). being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Claims 1-7 are under consideration in this Action.

Priority

Applicants' claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Specification

The disclosure is objected to because of the following informalities: The text contains two typos. On page 20, ¶2 the word Figure is spelled "Figur 2" and on page 30, l. 6, Biochem is not capitalized, "biochem Soc Trans".

Appropriate correction is required.

Claim Objections

Claim 3 objected to because of the following informalities: The claim would be more consistent with similar claims 2 and 4 if the claim recited a +1 frameshifting *event*. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harford (1995), Gene Expression, 4: 357-367 in view Bullock, et al. (1997), J Exp. Med, I 86:1051-1058 (of record), Ivanov et al. (1998) RNA 4: 1230-1238 and Mayrand et al. (1998) Immunology Today, 19(12) 551-556 (of record).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant claims are drawn to methods of testing a compound to alter recoding of a translational reading frame using a nucleic acid cassette and vector comprising a recoding causing sequence (+1 or -1 frameshift, stop codon readthrough or redefinition event) upstream from a MHC class I restricted epitope encoding sequence, which is in an alternate reading frame or downstream from a stop codon so that recoding of the recoding causing sequence is required fro the epitope to be expressed; infecting cells with the cassette vector; applying a compound and measuring efficacy of the compound to affect recoding by measuring activation of CD8+ T-cells specific for the epitope encoded by the epitope encoding sequence. Additional claims are drawn to specific recoding causing sequences that comprise a viral gene or a protein influencing cell proliferation.

Harford teaches various methods for discovering translational-targeted therapeutics where molecular targets related to translation are incorporated into a screen. Specifically, Harford teaches a "smart screen" wherein, for example, the HIV frameshifting sequence would be incorporated into a reporter gene with an easily detectable output, and the testing of a large number of substances to reveal agents that interfere with the function of the chosen target (e.g. the frameshifting sequence), see especially p. 364, col. 2., thus identifying therapeutics for retroviral diseases. Harford does not teach the details of a specific translation recoding detection assay.

Bullock et al. teach construction of recombinant variable initiation cassettes for the production of epitopes encoded in alternative RFs from a mutated influenza A PR/8/34 nucleoprotein (NP) gene. The authors utilize an internal AUG codon to rescue the presentation of three NP epitopes (NP_{50-57}, $NP_{147-155}$, $NP_{366-374}$) that had been shifted out-of-frame by a base deletion in the second codon of the NP open reading frame (ORF) (see for example the Abstract and Introduction). Recoding causing sequences (frameshifts) were introduced upstream from a MHC I restricted epitope (NP gene), where for example a +1 in the reading frame would cause a termination at codon 16 and no MHC I epitope production would occur unless a recoding of the recoding causing sequence occurs (see especially p. 1321, col. 2, ¶3). The nucleic acid cassette was inserted into an expression vector (vaccinia virus) and cells expressing an appropriate MHC class I molecule ($H\text{-}2^k$, $H\text{-}2^d$, or $H\text{-}2^b$) were infected (p. 1322, top of col. 1). Recoding events are measured in by activation of CD8+T cells using Cr release assays (see. p. 1322, Fig. 2 and Material and Methods). Recoding causing sequences embracing both +1 and –1 frameshifts were examined (claims 2 and 3, see especially all of p. 1322, col. 1). The recoding causing sequence comprises a sequence of a viral gene, influenza NP (claim 5), a premature stop codon (claim 6) and is considered, given broadest possible interpretation of the claims (claim 7) to comprise a sequence encoding a protein influencing cell proliferation (where production of nucleoprotein would have a negative effect on proliferation). Mayrand et al. additionally teach various types of translation mechanisms for generating non-traditionally derived CTL epitopes, including initiation codon scanthrough, re-initiation of translation, ribosomal

frameshifting, translation termination readthrough, internal initiation of translation, and doublet decoding (see especially p. 554, Table 3). Ivanov et al. further teaches application a compound in a translation recoding assay. Specifically, Ivanov teaches a chimeric gene construct comprising a frameshifting sequence from rat antizyme inserted between two reporter genes, GST and LacZ, where the antizyme ORF1 is fused in frame with the GST whereas the lacz is fused in the +1 frame so that lacz expression provides a measure of frameshifting. A comparison is made of frameshifing using the reporter cassette of the control relative to that where the polyamines putrescine or spermidine were added to the media (see especially p. 1232, col. 2 ¶¶ 4-5).

Given the teachings of the prior art, a person of skill in the art at the time of invention would have been motivated to combine the teachings of Harford for discovery of translation-targeted therapeutics for viral disease by screening compounds that affect translational recoding, for example that interfere with the HIV frameshifting sequence and therefore viral replication, by using the well described and highly sensitive CD8+ T-cell based recoding assay of Bullcok et al. The assay would provide an efficient means to test various compounds for efficacy to affect recoding, and thus identify novel drugs for anti-retroviral therapy. Thus, a skilled artisan would have been motivated, with every expectation of success, to combine the teachings of Harford, Bullock, Ivanof and Mayrand to create a smart screen based on the CD8+T translation recoding assay of Bullock for testing the effect of a compound on a recoding causing sequence, for example retroviral frameshifting sequences, and practice the instant claimed inventions to discover new therapeutics for viral diseases.

Pertinent Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Kollmus et al. (2000), Methods in Enzymology 318:363-374, discussing a frameshifting assay to characterize RNA-protein interactions, Reil et al (1993), J. Virol. 67(9): 5579-5584, discussing –1 ribosomal frameshifting within the slippery sequence from gag-pol interface of HIV-1, Malarkannan et al. (1999) Immunity, 10: 681-690, discussing out of frame peptide/MCH 1 complexes by recoded initiation codons and Hwang et al. (1994) PNAS 91: 5461-5465 discussing a +1 frameshift permitting synthesis of TK from a drug-resistant HSV mutant, and Taylor et al. (1994), J Med Chem, 34: 2637-2654, discussing pseudoknots which direct the synthesis of selenocysteine (SeC) containing –1 frameshift fusion proteins.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Guy Guidry, Ph.D. whose telephone number is 571-272-7928. The examiner can normally be reached on Monday through Friday 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Guy Guidry, Ph.D.

Examiner

Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER